



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,115	07/03/2003	Vladimir Baranov	079012-0102	7685
22428 7590 01/05/2009 FOLEY AND LARDNER LLP SUITE 500 3000 K STREET NW WASHINGTON, DC 20007			EXAMINER COOK, LISA V	
			ART UNIT 1641	PAPER NUMBER
			MAIL DATE 01/05/2009	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## REQUEST FOR RECONSIDERATION

### *Amendment Entry*

1. Applicants response to the Final Office Action mailed 06 August 2008 is acknowledged (paper filed 12/8/08). In the amendment filed therein claims 30-36 were canceled. Presently, claims 1-14, 20-27 and 29 are pending and under consideration.

## REJECTIONS MAINTAINED

### *Claim Rejections - 35 USC § 102*

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1-5, 20-21 and 23-25 are rejected under 35 U.S.C. 102(b) as anticipated by Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876).

Cais discloses a method and reagents for tagging biologically active material (column 7 lines 9-42) with metals (tag/label/transition elements). The metals include manganese (atomic number 25), silver (atomic number 47), gold (atomic number 79), Cobalt (atomic number 27), iron (atomic number 26), and nickel (atomic number 28). See Table 1. Accordingly the patent to Cais reads on Applicants claims regarding a transition element having an atomic number of 21-29, 39-47, 57-79 or 89. (See specification page 28 section 0122).

The metal (tag/label) is conjugated to the biologically active material (i.e. hapten or ligand) by an unnatural bound or covalent (chemical) bound. This reads on Applicant's claims regarding the direct tagging of a biological material. See column 8 line 36 through column 9 line 21 and column 10 lines 56-66. The metal or metal atoms can include linker moieties which facilitate specific binding (linker moiety). See column 9 lines 7-21. Competition formats are disclosed. See column 4.

The tagged biological active material (labeling substance and binding component) are mixed with a sample (ligand) to form a tagged complex. The bound complexes are separated from unbound material. Either the bound or unbound aliquot is measured for the metal content. Column 3 lines 5-22. The metal can be measured via a variety of detection systems including emission spectrophotometer. See column 6 lines 29-42.

Cais also teaches the detection/utility of any transition element/metal in specific binding assays and test pack kits (Applicant's kits with packaging means). See column 11 lines 45-66.

It is also worth noting that the printed matter on instructions merely teaches the use of an existing product, and thus cannot impart patentability. See *In re Ngai*, 5/13/04, Michel, Gajarsa, Linn, per curiam. In other words the printed matter on the instructions in a kit cannot serve to define the kit over the prior art. See *In re Gulack*, 217 USPQ (CAFC 1983).

Although Cais teaches the metal transition elements may be any metal element or combination of metal elements, Cais is silent with respect to isotopes. See column 11 lines 15-30. However, metal elements are known to exist as isotopes and be utilized to tag biological molecules. This is supported by US Patent #4,022,876 to Anbar.

Specifically, Anbar discloses a method of tagging antibodies or antigens (biologically active material) with stable isotopes of certain elements or long-lived radioisotopes of these elements (transition elements). Anbar et al. also teaches the detection of a transition element having an atomic number of 29. Specifically, Anbar et al. teach the utility of copper (atomic number 29). See column 2 lines 35-49. In one embodiment copper is combined with either iodide or selenide. In both instances the copper iodide or copper selenide are transition elements having or comprising the atomic number 29 element. See column 4 lines 11-15.

Accordingly it reads on Applicants claims regarding a transition element having an atomic number of 21-29, 39-47, 57-79 or 89. Antibody labeling (tagged biologically active material) is taught to produce higher sensitivity in immunoassay procedures. See column 6 lines 22-27.

Accordingly isotopes are deemed inherent to the teaching of any metal element or combination of metal elements by Cais. Column 11 lines 15-30.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Please see Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) as set forth above.

Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) differ from the instant invention in not specifically teaching reagent immobilization (bound to solid support).

However, Maggio disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186. The reagents can be bound to the solid support by covalent linkage or passive adsorption (non-covalent means). See page 187 1<sup>st</sup> paragraph. Maggio taught that solid supports such as test strips "are very convenient to wash thereby reducing labor in assay procedures". Page 186, last line.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to immobilize assay reagents on solid support surfaces as taught by Maggio in the assay method/reagents of Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) because Maggio taught that reagent immobilized solid supports "are very convenient to wash thereby reducing labor in assay procedures". Page 186, last line.

Absent evidence to the contrary the immobilization of reagents is deemed an obvious modification of Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876).

III. Claims 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) in view of Foster et al. (US Patent #4,444,879).

Please see Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) as set forth above.

Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) does not specifically teach kit configurations including standards and buffers. However, kits with standards and buffers are well known embodiments for assay reagents.

Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a microplate, positive controls, negative controls, standards, various buffers, and instructions are taught. The reagents are compartmentalized or packaged separately for utility. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay reagent kits taught by Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) and format them into a kits including standards and buffers because Foster et al. taught that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit.

Further, the reagents in a kit are available in pre-measured amounts, which eliminate the variability that can occur when performing the assay. Kits are also economically beneficial in reagent distribution.

IV. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) in view of Neilsen et al. (Spectrochimica Acta Part B, 53, 1998, 339-345).

Please see Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) as set forth above.

Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) differ from the instant invention in not teaching reagents for analyses related to laser ablation inductively coupled plasma-mass spectrometry and *gel electrophoresis*.

However, a procedure and reagents useful in inductively coupled plasma-mass spectrometry and further comprising electrophoresis is taught by Neilsen et al. Neilsen et al. employed both immunoelectrophoresis and laser ablation inductively coupled plasma (ICP)- mass spectrometry for the identification and quantification of metal binding proteins in blood serum.

Human serum was enriched with commercially available Co (Cobalt-supplied by Merck) was subjected to electrophoresis and the agarose gels corresponding to the 1<sup>st</sup> and 2<sup>nd</sup> dimensions were interrogated and analyzed using a Nd Yag laser (1064 nm) interfaced to ICP-mass spectrometry. See abstract, page 341 – 2.2.

Neilsen et al. taught that electrophoresis is a powerful separation procedure (page 340, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph) and laser ablation is a versatile solid sampling tool in ICP-spectrometry (page 340, 1<sup>st</sup> column, 3<sup>rd</sup> paragraph).



The combination provided a novel route for studying metal protein distribution in serum (peak response was linear with concentration and the method showed precise replication (6% RSD), with a detection limit of 0.29ng. See abstract and page 345 Conclusion.

With respect to the transition element or metal being positively charged or adapted to possess a positive charge, it is noted that Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) disclose the same transition metals as the ones claimed and Neilsen teaches the detection procedures as claimed. Absent evidence to the contrary, they necessarily teach the positive charged characteristic.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure transition elements (tags) linked to antibodies in the laser ablation inductively coupled plasma-mass spectrometry in combination with gel electrophoresis as taught by Neilsen et al. in the method/reagents because Neilsen et al. taught that the electrophoresis is a powerful separation procedure (page 340, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph) and laser ablation is a versatile solid sampling tool in ICP-spectrometry (page 340, 1<sup>st</sup> column, 3<sup>rd</sup> paragraph).

The combination provided a novel route for studying metal protein distribution in serum (peak response was linear with concentration and the method showed precise replication (6% RSD), with a detection limit of 0.29ng. See abstract and page 345 Conclusion.

One having ordinary skill in the art would have been motivated to do this to acquire the enhanced sensitivity, wherein accurate and precise detection is rapidly available.

V. Claims 22 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) in view of Crooke (WO 99/451450).

Please see Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) as set forth above.

Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) differs from the instant invention in not specifically teaching methods/reagents utilizing a plurality of tagged transition elements linked to a plurality of biologically active.

These limitations are taught in the methods/reagents of Crooke et al. Crooke et al. are drawn to mass spectrometric methods for biomolecular screening. See abstract. The method provides for screening ligand or combinatorial libraries of compounds against one or more than one biological target molecules. See abstract.

In other words the methods provide for the determining the interaction between one and a plurality of molecular species. See page 1, especially lines 17-19. In one embodiment different molecular weigh tags (distinguishable element tags) are utilized to detect different nucleic acid targets (biologically active materials). See page 10, line 19 for example.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure a plurality of biologically active materials bound to transition elements (tags) as taught by Crooke et al. in the method/reagents of Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876), because Crooke et al. taught that his method significantly accelerated screening efforts because multiple targets could be screened simultaneously against large numbers of compounds. See page 10 line 25-27. This would reduce processing time, allowing for more data on various compounds simultaneously.

#### ***Response to Arguments***

4. Applicants arguments filed 12/8/08 have been carefully considered but were not found persuasive.

Applicant contends that the rejections set forth in the Final Action dated 8/6/08 were previously presented and overcome. This argument was carefully considered but not found persuasive because the rejection under 35 U.S.C. 102(b) as anticipated by Cais (US Patent #4,205,952) supported by Anbar (US Patent #4,022,876) was not previously presented.

In the non-final mailed 10/20/06 and final mailed 6/5/07 the primary rejection was a 103(a) over Cais in view of Foster et al. In the non-final mailed 1/11/08 the primary rejection was a 102(b) as anticipated by Houk et al. In addition, the examiner may reconsider references and apply them to the modified claims and is not bound by previous positions.

Applicant has requested that the rejections of record and/or Finality of the action be withdrawn in order for Applicant to address any new issues raised by the Examiner. This request has been carefully considered but not found persuasive because no new issues have been raised by the Examiner. In fact, the rejections of record are maintained for compact prosecution as not to present piecemeal analysis of the instant invention. (As requested by Applicant on page 6 of the response filed 12/8/08).

***Rejection over 102(b)***

Applicant contends that Cais does not teach all the elements of the claim. In particular, while Cais disclosed tagging a biological material with a transition element and detection of the tag, it does not teach methods of evaluation that can distinguish isotopes. This argument was carefully considered but not found persuasive because Cais is cited with Anbar to support isotope tags. Although Cais teaches the metal transition elements may be any metal element or combination of metal elements, Cais is silent with respect to isotopes. See column 11 lines 15-30. However, metal elements are known to exist as isotopes and be utilized to tag biological molecules. This is supported by US Patent #4,022,876 to Anbar. Specifically, Anbar discloses a method of tagging antibodies or antigens (biologically active material) with stable isotopes of certain elements or long-lived radioisotopes of these elements (transition elements). Anbar et al. also teaches the detection of a transition element having an atomic number of 29. Specifically, Anbar et al. teach the utility of copper (atomic number 29). See column 2 lines 35-49. In one embodiment copper is combined with either iodide or selenide.

Applicant argues that the detect of isotopes requires a more discriminate method of detection which is not taught by Cais (i.e. mass spectroscopy). This method was carefully considered but not found persuasive because the instant claims are not drawn to methods of detection but kits including tagged materials. The utility of the kits is not given patentable weight to the products.

Applicant contends that the rejection over Cais supported by Anbar disclose negative ion detection. This argument was carefully considered but not found persuasive because the rejected claims do not require a positive ion. Claims 1-5, 20-21 and 23-25 merely require at least one tag comprising at least one isotope of a transition element and a linker. There is no requirement in the body of the claim for a ***positive ion***.

***The cited references were improperly combined***

Applicant argues that Cais as supported by Anbar cannot be combined because Anbar teaches a completely different tag and detection procedure. This argument was carefully considered but not found persuasive because both patents are drawn to compositions useful as tags for biological materials and methods for the measurement of such tags. Applicant argues that the method of Anbar measures the negative ion but not the positive ion (Cu) although the two are bound to a molecule of interest. This argument was not found persuasive because the instant claims utilize open language comprises and therefore can read on compositions having combined tags (Cu with another tag like iodide/selenide).

Art Unit: 1641

With respect to the rejections including Maggio, Foster, Neilsen, and Crooke; Applicant contends that the references do not cure the deficiencies of Cais as supported by Anbar and should be withdrawn. This argument has been carefully considered but not found persuasive. Cais supported by Anbar has been reconsidered and maintained. Accordingly the rejections including Maggio, Foster, Neilsen, and Crooke are maintained.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The recitation that the transitional element is *positively charged* in the preambles of the claims has not been given patentable weight because it has been held that a preamble is denied the effect of a limitation where the claim can otherwise stand alone. *In re Ridden*, 318 F.2d 761, 138 USPQ 112; *In re Maeder*, 337 F.2d 875, 143 USPQ 248.

5. For reasons aforementioned, no claims are allowed.
6. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week.

Art Unit: 1641

In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, can be reached on (571) 272-0806.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*Lisa V. Cook*  
*Remsen*  
*(571) 272-0816*  
*12/31/08*

/Lisa V. Cook/  
Primary Examiner, Art Unit 1641